

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the claims:

1. (Currently amended) A method for screening compounds useful for the treatment of proliferative and differentiative disorders comprising contacting a compound with a cell or a cell extract expressing ~~either Cks1 and Skp2, or Cks1, p27 and Skp2~~, and detecting a change in the activity of Skp2 Skp2 binding activity or Skp2 ubiquitin ligase activity.
2. (Currently amended) The method of Claim 1 wherein the change ~~in the activity of Skp2~~ binding activity is detected by detecting a change in the ~~interaction~~ binding of Skp2 with either p27 or Cks1.
3. (Currently amended) The method of Claim 1 wherein the change in the ~~activity of Skp2~~ ubiquitin ligase activity is detected by detecting a change in the ubiquitination ~~of p27 or~~ degradation of ~~p27 or Cks1~~ a Skp2-specific substrate.
4. (Currently amended) A method for screening compounds useful for the treatment of proliferative and differentiative disorders comprising adding a compound ~~in a purified system to a mixture~~ containing ~~either Cks1 and Skp2, or Cks1, p27 and Skp2~~, and detecting a change in the activity of Skp2 Skp2 binding activity or Skp2 ubiquitin ligase activity.
5. (Currently amended) The method of Claim 4 wherein the change ~~in the activity of Skp2~~ binding activity is detected by detecting a change in the ~~interaction~~ binding of Skp2 with either p27 or Cks1.
6. (Currently amended) The method of Claim 4 wherein the change in the ~~activity of Skp2~~ ubiquitin ligase activity is detected by detecting a change in the ubiquitination ~~of p27 or~~ degradation of ~~p27 or Cks1~~ a Skp2-specific substrate.
7. (Currently amended) A method for screening compounds useful for the treatment of proliferative and differentiative disorders comprising:

- (a) adding a compound ~~in a purified system~~ to a mixture containing Skp2 and one or both of: (i) a polypeptide corresponding to the carboxy terminus of the human p27 chain having the sequence NAGSVEWTPKKPGLRRRQT (SEQ. ID. NO: 91) with or without a phosphothreonine at position 8 and (ii) Cks1; and
- (b) detecting a change in the ~~activity of Skp2~~ interaction of Skp2 with Cks1 or the polypeptide.

8. (Currently amended) The method of Claim 7 wherein the change in the ~~activity of Skp2~~ interaction of Skp2 with Cks1 or the polypeptide is detected by detecting a change in the ~~interaction~~ binding of Skp2 ~~with~~ to either the polypeptide or Cks1.

9. (Currently amended) The method of Claim 7 wherein the change in the ~~activity of Skp2~~ interaction of Skp2 with Cks1 or the polypeptide is detected by detecting a change in the ubiquitination ~~of the polypeptide~~ or degradation of the polypeptide ~~or Cks1~~.

10. (New) A method for screening compounds useful for the treatment of proliferative and differentiative disorders comprising:

- (a) adding a compound ~~in a purified system~~ to a mixture containing Skp2 and one or both of: (i) a polypeptide corresponding to the carboxy terminus of the human p27 chain having the sequence NAGSVEWTPKKPGLRRRQT (SEQ. ID. NO: 91) with or without a phosphothreonine at position 8 and (ii) Cks1; and
- (b) detecting a change in Skp2 ubiquitin ligase activity.

11. (New) The method of Claim 10 wherein the change in Skp2 ubiquitin ligase activity is detected by detecting a change in the ubiquitination or degradation of the polypeptide or a Skp2-specific substrate.

12. (New) The method of Claim 3, 6, or 11 wherein the Skp2-specific substrate is p27.

13. (New) A method for screening compounds useful for the treatment of proliferative and differentiative disorders comprising contacting a compound with a cell or a cell extract

expressing Cks1, p27 and Skp2, and detecting a change in Skp2 binding activity or Skp2 ubiquitin ligase activity.

14. (New) The method of Claim 13 wherein the change in Skp2-binding activity is detected by detecting a change in the binding of Skp2 with either p27 or Cks1.

15. (New) The method of Claim 13 wherein the change in the Skp2 ubiquitin ligase activity is detected by detecting a change in the ubiquitination or degradation of p27.

16. (New) A method for screening compounds useful for the treatment of proliferative and differentiative disorders comprising adding a compound ~~in a purified system~~ to a mixture containing Cks1, p27 and Skp2 and detecting a change in Skp2 binding activity or Skp2 ubiquitin ligase activity.

17. (New) The method of Claim 16 wherein the change in Skp2-binding activity is detected by detecting a change in the binding of Skp2 with either p27 or Cks1.

18. (New) The method of Claim 16 wherein the change in the Skp2 ubiquitin ligase activity is detected by detecting a change in the ubiquitination or degradation of a Skp2-specific substrate.

19. (New) The method of Claim 16 wherein the Skp2-specific substrate is p27.

20. (New) The method of Claim 1 or 13 wherein the cell or cell extract further expresses Cyclin E and Cdk2.

21. (New) The method of Claim 4, 7, 10, or 16 wherein the system further contains Cyclin E and Cdk2.